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Brachytherapy in an advanced stage of pancreatic cancer - a case report

Witold Kycler[1], Marek Teresiak[1], Janusz Skowronek[2], Piotr Łaski[1]

Treatment options for pancreatic cancer remain limited due to the large proportion of patients presenting with advanced disease at the time of diagnosis. Literature reports emphasize the advantages arising from palliative treatment using HDR brachytherapy.The promising results have provided encouragement for extending the application of this method. Neoadjuvant therapy may stop tumor growth or induce regression of local tumor advancement. We present a case of a patient with locally advanced pancreatic cancer treated with interstitial brachytherapy at the Greatpoland Cancer Centre in Poznań.

Brachyterapia w zaawansowanym raku trzustki – opis przypadku

Rak trzustki rozpoznawany jest zwykle w późnych stopniach zaawansowania klinicznego. Ogranicza to w znacznym stopniu możliwości zastosowania radykalnego leczenia chirurgicznego. Aktualnie coraz częściej stosuje się brachyterapię HDR jako leczenie paliatywne w zaawansowanych rakach trzustki. Leczenie neoadjuwantowe oparte na brachyterapii HDR stwarza w niektórych przypadkach możliwość zahamowania wzrostu guza i zmniejszenia miejscowego zaawansowania. Przedstawiamy opis leczenia pacjenta z miejscowo zaawansowanym rakiem trzustki, u którego zastosowano brachyterapię HDR.

Key words: pancreatic cancer, HDR brachytherapy
Słowa kluczowe: rak trzustki, brachyterapia HDR

Introduction

Every year about 3200 new cases of pancreatic cancer are registered in Poland. A considerable percentage of patients (85-90%) commence treatment in advanced stages of disease [1] and relative five-year survivals after radical surgical resection reach about 10 %. [2]. According to the literature data patients with unresectable pancreatic adenocarcinoma die within 6 months after the operation [2,3].

Radical surgical resection is the treatment of choice. Unfortunately, radical treatment cannot be applied to a majority of patients as they are already in advanced stages of the disease. For this very reason treatment options for pancreatic cancer remain limited. Chemo-radiotherapy, palliative surgery and brachytherapy are considered as testable treatment concepts for locally advanced pancreatic cancer [3-6].

Unresectable pancreatic cancers are very difficult to treat with external beam therapy alone, due to the proximity of adjacent normal organs and the high doses required to effectively irradiate these neoplasms [7].

Brachytherapy is one of the most efficient palliative methods of treatment. It diminishes pain, reduces tumor--mass effect and slows the growth of the tumor.

Indications for HDR brachytherapy are:
- palliative treatment (in a majority of cases) [4, 7],
- presurgical treatment (to induce regression of locally advanced cancers) [5],
- postsurgical treatment with catheters implanted into the residual mass of the tumour [2, 9],
- radical treatment (in some individual cases) combined with external beam radiotherapy and/or chemotherapy [6-9].

Perioperative permanent implantation of ^{125}I or ^{123}Pd is being investigated as a method applied to unresectable tumors at the time of laparotomy [10-12]. Bypass procedures often accompany implantation and external beam radiation usually follows. In case of patients with unresectable tumors the disease has to be confined to the pancreas with the tumor less than 5-6 cm in size. Perioperative HDR irradiation of pancreatic cancers through plastic tube implantations is also being explored as a means of increasing the dose to an unresectable lesion [6, 13].

The efficacy of brachytherapy, as compared with the efficacy of external beam alone, may be attributed to the possibility of delivering a higher concentrated radiation dose to the tissues with more precision, thus improving lo-

[1] 2nd Department of Oncological Surgery
[2] 1st Department of Radiotherapy
Greatpoland Cancer Center, Poznań

cal control, provided that the tissue is clinically delimitable and accessible. At the same time, the surrounding healthy tissues are spared. In contrast to external-beam irradiation, brachytherapy is invasive as it requires the insertion of site-specific applicators under sedation or anaesthesia.

We present a case of a patient with locally advanced pancreatic cancer who had been treated with interstitial brachytherapy at the Greatpoland Cancer Centre, Poznań.

Case report

A 79- year old man was admitted with an 8-month history of recurrent varices haemorrhoidales inflammation. The patient suffered from occasional presence of myxomatous stools. He had no serious illness before that.

He was in good general condition, free of symptoms suggesting neoplastic disease. Abdominal ultrasound (performed 6 months before treatment), colonoscopy and double contrast method colon exam were normal. Rectoscopy revealed varices haemorrhoidales. The patient was qualified for surgery due to recurrent varices haemorrhoidales inflammation.

In March 2000 he was admitted to the Greatpoland Cancer Center, 2nd Department of Oncological Surgery in Poznań. Presurgical exams were ordered. The abdominal ultrasound showed a solid 5 cm tumour in the head of pancreas. Hematological and biochemical tests, chest X-ray and double contrast colon exam were normal. There was no evidence of extrapancreatic spread of the disease. Cytological diagnosis by fine needle aspiration under CT control was performed, providing a diagnosis of cellulae carcinomatosae – adenocarcinoma.

The patient was qualified for surgery. A 5 cm-diameter tumor was discovered in the head of the pancreas during laparotomy. There was no evidence of metastatic disease in the abdomen. On intraoperative estimation the tumor was pronounced unresectable.

During surgery three parallel "blind-end" intratissual catheters were implanted into the tumor mass at 1 cm distances.

Brachytherapy was started on the second day after the operation. IBU (Integrated Brachytherapy Unit) check photos were made and imaging information was transferred to the treatment planning computer via an information network. The target volume contained the tumor mass with a 1 cm margin (85% isodose of reference dose). PLATO planning system was used.

For HDR brachytherapy a microselectron HDR unit was used, with Iridium 192 as the radioactive source – 10 Ci activity.

The patient received 10 fractions of 3 Gy daily, total dose reaching 30 Gy. Treatment tolerance was good and no complications were observed. Recovery was uncomplicated and the patient was discharged on the 14-th day after surgery.

From then on the patient remained under the care of a family doctor and did not report to our hospital. 14 months after surgery and brachytherapy the patient observed disturbances reported as alternate diarrhoea and constipation.

Abdominal ultrasound revealed liver with steatosis – solid, heterogenous, without disintegration features with non-extended bile ducts and a tumor of 4-5 cm in diameter localized in the head of pancreas. Intra-abdominally, on the right hand side the colon (caecum) wall was thickened (reaching 18 mm) and stiffened over a distance of some 6 cm (Tu coeci). The family doctor advised palliative treatment.

Four months later, in October 2001, the patient reported to the Greatpoland Cancer Center with the above-mentioned complaints.

The abdominal ultrasound showed hyper- and hypoechogenic, meta-characteristic focuses in the right lobe of the liver. Laboratory test revealed an increased CEA – 500 ng/mL (normal value below 3,0 ng/mL).

Because of subileus, the patient was immediately admitted and qualified for laparotomy (10.2001). A movable tumor was discovered in the caecum during laparotomy. Separate metastatic tumours were found in the liver. The tumour originating from the head of the pancreas infiltrated the back wall of the duodenum. Right hemicolectomy was performed.

The operation was palliative in its character. The post operative course was uncomplicated and the patient was discharged on day 18 after surgery.

The pathology report revealed adenocarcinoma tubulopapillare (G2), infiltratio carcinomatosa profunda tunicae muscularis propriae et serosae coli et telae adiposae pericolicae, lymphonodulitis reactiva No XV, G2, Dukes B, Astler Coller B2, pT3. The tumour infiltrated over the entire wall of the small intestine.

The last medical examination was performed 3 months after surgery: the patient was generally in quite good condition, able to move, free of pain and with the wound completely healed.

The entire observation time from pancreatic cancer diagnosis reached 24 months.

Discussion

Non-specific symptoms of pancreatic cancer delay the diagnosis. The conventional triade – epigastric pain, weight loss and icterus appear in advanced stages of pancreatic tumours. Usually the first symptom is a perceptible abdominal mass in the epigastrium or a tumor accidentally detected during ultrasonography. Other symptoms, such as non-specific pains in the upper abdomen, loss of appetite, diabetes and psychological disturbances are obviously non- characteristic. In a few cases one may additionally observe symptoms connected with hypertension in the inferior caval vein.

Locally advanced cancer estimated on surgery renders radical excision impossible. Brachytherapy provides promising results – tumor progression may be stopped.

The patient, whose case we report, didn't report any pain. Also no alimentary tract dysfunction nor icterus

were reported. At the time when the patient reported with symptoms of a second cancer his quality of life as a pancreatic cancer survivor was good [14]. The survival expectancy in case of advanced, unresected pancreatic cancer (clinical stage III and IV) is, approximately, six months [3, 10].

Different authors report the advantages of palliative treatment with HDR brachytherapy. The satisfactory results of this method have widened the application of this method. Neoadjuvant therapy has the potential to induce regression of locally advanced cancers and render them resectable.

Wanebo and al. [5] used preoperative chemoradiotherapy as a testable treatment concept for locally advanced pancreatic cancer. Fourteen surgically staged patients with locally advanced pancreatic cancer, disqualified from radical surgery, were treated by preoperative chemotherapy. After treatment, they were qualified for re-exploration and resection. 81 % (9 patients) underwent pancreatic resection including standard Whipple resection, resection of body and neck and extended resection. The histopathology examination indicated complete pathologic response in two patients, one patient had no residual cancer, another (who had iridium 192 brachytherapy) had normal core biopsies of the pancreatic head, and five others had incomplete pathologic response. All 9 patients achieved 5-year survival.

Pfreungner and al. [3] have presented clinical reports of 19 patients with unresectable pancreatic cancer. 9 women and 10 men underwent interstitial brachytherapy. Distribution according to UICC stages has shown 4,10 and 5 patients in stages II to IV, respectively. A total dose of 10 to 34 Gy to the reference isodose was delivered (single dose – 1.88 to 5 Gy). Brachytherapy was followed by external beam therapy, delivering an additional dose of 40 to 58 Gy. Median survival time was 6 months, local control rate was 70%. Brachytherapy treatment was well tolerated, severe acute side effects were not observed. Authors concluded, that ^{192}Iridium brachytherapy is comparable to IORT (intraoperative radiotherapy) or seed implantation.

These good results of brachytherapy are a sufficient cause for the further development of this method. Intratumoral infusional brachytherapy using macroaggregated human albumin in combination with radioactive chromic phosphate (32P) extends the possibility to administer brachytherapy to tumors, the location of which makes it impossible to implant catheters [2, 9].

In the presented case the main clinical problem arose from the fact that the patient with a non-resectable pancreatic cancer developed a second malignancy.

During the four months after the diagnosis of the second malignancy the patient was not referred for surgery. In June 2001 abdominal ultrasound provided symptoms of a caecum tumor with evidence of healthy liver parenchyma. On admission to the surgery department the abdominal ultrasound revealed a metastatic liver. The clinical advance of caecum cancer rendered radical surgical treatment impossible and the patient's condition deteriorated.

During the 24 months after the onset of pancreatic cancer treatment we achieved good results of palliative treatment. We didn't observe any side effects after brachytherapy. The development of the second cancer and postponed surgical treatment caused progression of the caecum cancer which, in due time, metastasied.

We believe that combining surgery and brachytherapy in the treatment of locally advanced pancreatic cancer is an efficient and safe palliative treatment method.

Witold Kycler MD
2nd Department of Oncological Surgery
Greatpoland Cancer Center
ul. Garbary 15
61-866 Poznań, Poland

References

1. Szawłowski AW. Nowotwory górnego odcinka przewodu pokarmowego. Rak trzustki. In: Krzakowski M, Siedlecki P (eds). *Standardy leczenia systemowego nowotworów złośliwych u dorosłych w Polsce*. Warszawa: Grupa Multimedialna 1999; 61-4.
2. Westlin JE, Andersson-Forsman C, Garske U et al. Objective responses after fractionated infusional brachyterapy of unresectable pancreatic adenocarcinomas. *Cancer* 1997; 15; 80: 2743-8.
3. Pfreundner L, Baier K, Schwab F et al. 3D-Ct-planned interstitial HDR brachytherapy + percutaneous irradiation and chemotherapy in inoperable pancreatic cancer. Methods and clinical outcome. *Strahlenther Onkol* 1998; 174: 133-41.
4. Dobelbower RR, Montemaggi P. Brachytherapy for pancreatic cancer: a review. *Hepatogastroenterology* 1996; 43: 333-7.
5. Wanebo HJ, Glicksman AS, Vezeridis MP et al. Preoperative chemotherapy, radiotherapy, and surgical resection of locally advanced pancreatic cancer. *Arch Surg* 2000; 135: 81-8.
6. Schuricht AL, Spitz F, Barbot D et al. Intraoperative radiotherapy in the combined-modality management of pancreatic cancer. *Am-Surg* 1998; 64: 1043-9.
7. Erickson B, Wilson JF. Clinical Indications for Brachythapy. *J Surg Oncol* 1997; 65: 218-227.
8. Bodner WR, Hilaris BS, Mastoras DA. Radiation therapy in pancreatic cancer: current practice and future trends. *J Clin Gastroenterol* 2000; 30: 230-3.
9. DeNittis AS, Stambaugh MD, Lang P et al. Complete remission of nonresectable pancreatic cancer after infusional colloidal phosphorus-32 brachytherapy, external radiation therapy, and 5-fluorouracil: preliminary report. *Am J Clin Oncol* 1999; 22: 355-60.
10. Raben-A, Mychalczak B, Brennan MF et al. Feasibility study of the treatment of primary unresectable carcinoma of the pancreas with 103Pd brachytherapy. *Int J Radiat Oncol Biol Phys* 1996; 35: 351-6.
11. Nori D, Merimsky O, Osian AD et al. Palladium-103: a new radioactive source in the treatment of unresectable carcinoma of the pancreas: a phase I-II study. J Surg Oncol 1996; 61: 300-5.
12. Mohiuddin M, Rosato F, Barbot D et al. Long-term results of combined modality treatment with I-125 implantation for carcinoma of the pancreas. *Int J Radiat Oncol Biol Phys* 1992; 23: 305-11.
13. Warszawski N, Pfreunder L, Bratengeier K, et al. HDR interstitial therapy for pancreatic carcinoma. *Brachytherapy J* 1992; 6: 9-94.
14. Order SE, Siegel JA, Principato R et al. Selective tumour irradiation by infusional brachytherapy in nonresectable pancreatic cancer: phase I study. *Int J Radiat Oncol Biol Phys* 2001; 50: 279.

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